AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings of claims in the application:

LISTING OF CLAIMS:

1-116. (cancelled)

- 117. (new) A transgenic mouse whose genome comprises a homozygous disruption in an endogenous Serca2 gene in heart cells following expression of a site-specific recombinase of heterogenous origin, wherein the disruption of the endogenous Serca2 gene results in a lack of expression of a functional Serca2 protein in the heart cells.
- 118. (new) The transgenic mouse of claim 117, wherein the mouse exhibits one or more of defective Ca^{2+} handling, reduced Ca^{2+} pumping ability, decreased heart contractility and heart failure.
- 119. (new) The transgenic mouse of claim 117, wherein the disruption is a null mutation of the endogenous Serca2 gene.
- 120. (new) The transgenic mouse of claim 117, wherein the heart cells are in the heart ventricle.

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- 121. (new) The transgenic mouse of claim 117, wherein the genome further comprises the gene encoding the heterogenous recombinase.
- 122. (new) The transgenic mouse of claim 117, wherein the recombination enzyme is Cre recombinase.
- 123. (new) The transgenic mouse of claim 121, wherein the recombinase is encoded by a recombinase gene that is under transcriptional control of a heart cell specific regulatory promoter.
- 124. (new) The transgenic mouse of claim 121, wherein the recombinase is inducible.
- 125. (new) The transgenic mouse of claim 124, wherein the recombinase is inducible by tamoxifen.
- 126. (new) The transgenic mouse of claim 123, wherein the recombinase is encoded by a MerCreMer gene.
- 127. (new) The transgenic mouse of claim 123, wherein the promoter is an alpha-myosin heavy chain (α -MHC) promoter.

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- 128. (new) The transgenic mouse of claim 117, wherein the mouse is an adult mouse.
- 129. (new) The transgenic mouse of claim 117, wherein the recombinase is expressed in the mouse heart tissue.
 - 130. (new) The transgenic mouse of claim 117,

wherein both of the endogenous Serca2 genes are modified by two loxP recombination sites positioned within introns of the Serca2 gene, the two loxP recombination sites flanking exons 2 and 3 of the Serca2 gene, and

the genome further comprises a MerCreMer gene encoding a recombinase under transcriptional control of an $\alpha\text{-MHC}$ promoter.

- 131. (new) A cell isolated from the transgenic mouse of claim 117.
- 132. (new) The cell of claim 131, wherein the cell lacks expression of a functional Serca2 protein.
- 133. (new) The cell of claim 131, wherein the cell is a heart cell.
- 134. (new) A method of screening a compound for activity against heart failure, comprising:

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administering the compound to the transgenic mouse according to claim 117;

observing one or more effect of the compound in the mouse.

- 135. (new) The method of claim 134, wherein the one or more effect is selected from the list consisting of improvement in general condition, alleviation of symptoms, reduced lethality and improvement of heart contractility.
- 136. (new) A method of screening a compound for activity against defective Ca^{2+} handling, comprising:

administering the compound to the transgenic mouse according to claim 117;

measuring a difference in Ca²⁺ handling in the transgenic mouse before and after administering the compound.

- 137. (new) A method of studying heart failure, comprising disrupting the endogenous Serca2 gene in the heart cells of the transgenic mouse of claim 117, wherein the disruption is homozygous.
- 138. (new) A method for creating the transgenic mouse of claim 117, comprising:

breeding a first transgenic mouse whose genome comprises a modified endogenous Serca2 gene, the Serca2 gene being modified

by one or more heterogenous recombination site inserted in the Serca2 gene, with a second transgenic mouse whose genome comprises an inducible recombinase gene, the recombinase being expressed in the heart cells when induced;

obtaining an offspring mouse whose genome comprises the modified endogenous Serca2 gene and the inducible recombinase gene; and

inducing the recombinase in the offspring mouse to activate site-specific recombination and disrupt the endogenous Serca2 gene in the heart cells.

- 139. (new) The method of claim 138, wherein the recombinase is encoded by a MerCreMer gene.
- 140. (new) The method of claim 138, wherein the recombinase is inducible by administering tamoxifen to the mouse.
- 141. (new) A transgenic mouse whose genome comprises a homozygous disruption of an endogenous Serca2 gene in heart cells resulting in a lack of expression of functional Serca2 protein in the heart cells.